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An Overview On Niosome As Carrier In Dermal Drug Delivery

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Abstract:

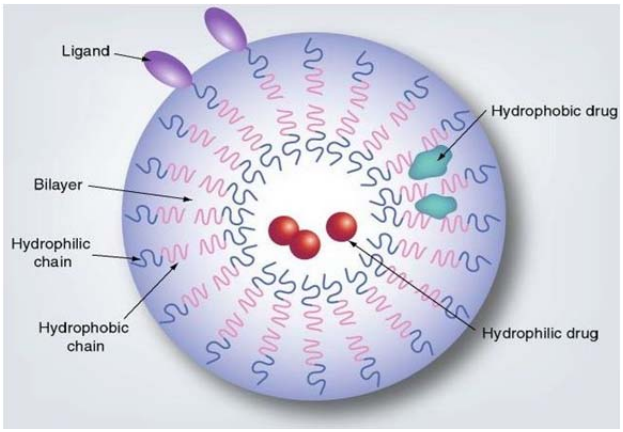
Niosome is used as a colloidal vesicular carrier in drug delivery. It is made up of non-ionic surfactant vesicles which are biodegradable and non-toxic. It is cost effective and stable compared with other colloid carriers. It has applications in oral, topical, parental and novel drug delivery as controlled and targeted delivery. In earlier 70's the niosomes were used in the field of cosmetics. Lancome launched an anti-ageing niosomal cream in 1986. In novel drug delivery it has applications on treatment of cancer, used as a carrier in hemoglobin, delivery of the peptide drugs through oral route, in treatment of leishmaniasis, in ophthalmic delivery, in cosmetics and as carrier in dermal drug delivery. This review article focuses on niosome structure, composition, advantages, types of niosomes, methods of preparation, characterization and its application. It also deals in detail about the role of niosome as a carrier in dermal drug delivery.

Key Words : Niosomes, application, dermal carrier

INTRODUCTION:

Drug targeting is the release of drug in a specific site for its maximum therapeutic action with reduced toxicity .Vesicular drug delivery releases the encapsulated drug from the vesicle to the target site. Vesicular carriers are used for drug targeting, release of drug in controlled manner and also to enhance the permeation of drugs which has low percutaneous penetration. Now day's niosomes are used as carriers in the topical preparation, which has the property of carrying both hydrophilic and lipophilic drugs.[1] Niosomes (non ionic surfactant vesicles) are microscopic lamellar structure. They are formed on addition of non toxic surfactant of the alkyl or dialkyl polyglycerol ether class and cholesterol followed by the subsequent hydration in aqueous media.]Niosomes can be SUV (small unilamellar vesicles), MLV (Multi lamellar vesicles) or LUV (large unilamellar vesicles).[2]Surfactant based colloidal vesicle carrier noisome can be used as an efficient dermal drug delivery since it has a targeted, controlled and enhances the permeation of the drug through dermal route. Niosome are stable and less irritation during its action on dermal route compared to other colloidal vesicle carrier. Skin acts as a barrier for the penetration of drugs. Epidermis has the outermost layer called the stratum corneum which acts as the rate limiting step for the percutaneous absorption of drug.[3]The physico-chemical properties of a drug play an important role in the penetration of drugs through the stratum corneum. Once the drug compound gets transferred into the epidermis, they are carried to the deeper tissues by dermal blood circulation. The partition co-efficient and the diffusion co-efficient of the drug are important for the penetration of drugs into proteins (or) lipid region. Hence better penetration of transdermal drug delivery is achieved by niosomal vesicles.[4]

STRUCTURE OF NIOSOME:



COMPOSTITION OF NIOSOME:

Niosomes are composed of

CHOLESTROL: It gives proper shape and rigidity to the niosomes.

NON-IONIC SURFACANT: The non-ionic surfactant contains hydrophilic head and hydrophobic tail. The most of non-ionic surfactants used are Span (60,40,80), Tween (20,40,80), Brij (52,58,35,30), Alkyl Amides, Sorbitan ester, Ester linked surfactants.[5]

Advantages:

- It gives controlled and targeted drug delivery.
- Economically cheap colloidal vesicle carrier.
- It states good patient compliance.
- Stable when compared with liposomes.
- Both hydrophilic and hydrophobic drugs can be prepared by niosomes.
- The penetration of drugs can be enhanced in dermal drug delivery.
- Osmotically active and stable increases the stability of entrapped drug.
- Special requirements are not required for the storage of surfactants.[6]

TYPES OF NIOSOMES:

Niosomes are classified based on number of bilayer, size and method of preparation.

Mulitlamellar- 0.5µm to 10µm in diameter.

Larger unilamellar- 0.1µm to 1µm in diameter

Small unilamellar – 25-500nm in diameter.

PRONIOSOMES:

These are the niosomal formulation made up of carrier and surfactants, which are to be hydrated before use

Carrier + surfactant = Proniosomes

Proniosomes + Water = Niosomes

BOLA SURFACTANT CONTAINING NIOSOME:

They are special type of surfactants made up of omegahexadecylbis-(1-aza-18crow-6) : Span80: cholesterol in 2:3:1 ratio.[7]

ASPASOMES:

Aspasomes are the vesicles made up of acorbyl palmitate, cholesterol and highly charged lipid such as diacetyl phosphate. To obtain niosomes, the aspasomes are first hydrated with aqueous solution and then sonicated. These are mainly used in dermal drug delivery to enhance the permeation of drugs.

VESICELS IN WATER AND OIL SYSTEM (V/W/O):

The formation of the v/w/o is done by adding suspension of niosomes into the oily phase at 60°C. It forms a gel like consistency it can entrap the hydrophilic active ingredients. These vesicles are used in controlled drug delivery.

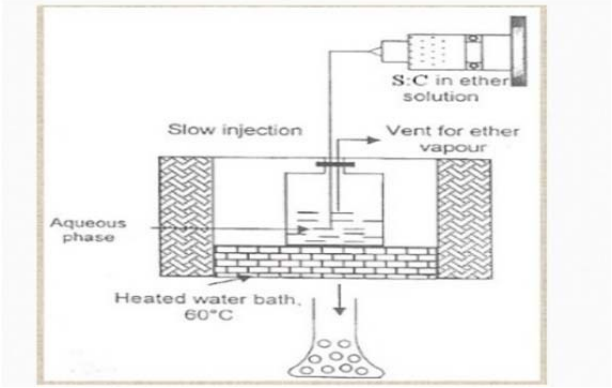
DEFORMABLE NIOSOMES:

The mixture of non-ionic surfactants, ethanol and water forms the deformable niosomes. These are smaller vesicles and easily pass through the pores of stratum corneum, which leads to increase penetration efficiency. It can be used in topical preparation.[8]

METHOD OF PREPARATION:

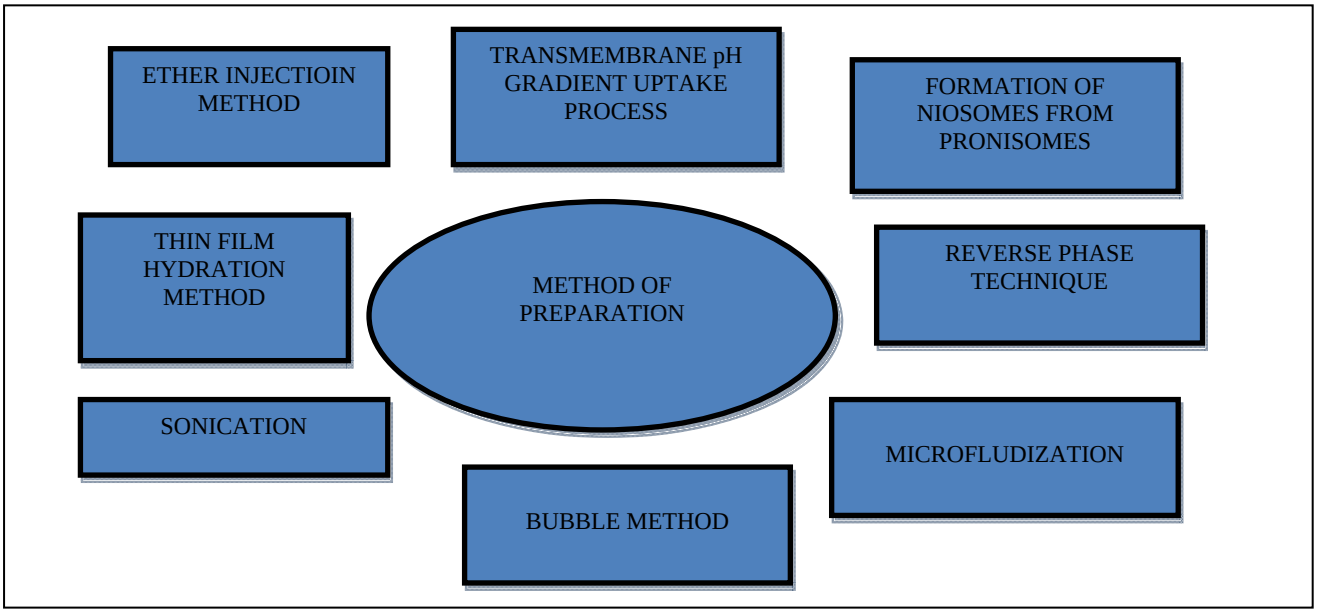
ETHER INJECTION METHOD:

In this method the lipid layer cholesterol and the non-ionic surfactants are dissolved in the organic solvent like diethyl ether. This solution was injected slowly through a 14 guage needle into an aqueous solution (drug solution) which was preheated to 60°C. The ether solution was evaporated using rotary evaporator, after evaporation of the organic solvent it forms single layered vesicles. The size of the vesicles formed ranges from 50-1000nm.



THIN FILM HYDRATION METHOD:

In this method the components of niosomes are dissolved in a organic solvents (chloroform, diethyl ether) which is taken in a round bottom flask. The organic solvent is evaporated using rotary evaporator. It forms a thin film inside the flask. The dried film is hydrated by adding aqueous solution (containing drug) by gentle agitation it forms a milky niosomal dispersion. Large multilamellar niosomes are formed.[9]



SONICATION:
The mixture of cholesterol and the surfactant are dispersed in an aqueous solution. The solution is transferred to a vial and probe sonicated at 60°C for 3mins. The titanium probe is used for sonication. Multilamellar vesicles are formed by this method.

REVERSE PHASE TECHNIQUE:
The cholesterol and surfactant of equal ratio is been dissolved in a mixture of organic solvent (ether & chloroform). An aqueous phase which contains drug is added to the above phase it forms a mixture of two phases. The phase is sonicated at 4-5°C and it forms a clear gel, it is further sonicated by adding small amount of PBS (phosphate buffer solution). The organic phase is removed by suing rotary vacuum evaporator at 40-60°C. The resulting viscous noisome suspension is diluted with PBS solution in a water bath at 60°C for 10 mins to yield niosomes.

BUBBLE METHOD:
It is a one step preparation method for the niosomes. Organic solvents are not used in this method. The bubbling unit contains round bottom flask with 3 necks positioned in the water bath. Water- cooled reflex is in the first neck, the thermometer is in the second neck to the check the temperature and the third neck for the nitrogen supply. The cholesterol and surfactant is dispersed in the buffer (7.4) at 70°C. The dispersed mixture is mixed for 15sec with high shear homogenizer and immediately afterwards bubbled at 70°C using nitrogen gas.[10]

NIOSOMES VS LIPOSOMES:
The liposomes and niosomes are relatively similar in nature. The phospholipids used in liposomes are not stable in nature; whereas niosomes are made up of non-ionic surfactants are stable. Niosomes are prepared from unchanged single chain non-ionic surfactant, whereas liposomes are prepared from double-chain phospholipids. The size of niosomes ranges from 10-100nm and liposomes from 10-300nm. According to cost, the niosomes are economically cheap compared to liposomes.[11]

CHARACTERIZATION:
FTIR:
The FTIR study is carried put to find out whether any interactions are there between the drug and the exipients used in the formulation.
SIZE, SHAPE AND MORPHOLOGY:
The structure of the noisome can be identified by using SEM/TEM. The size that is the diameter of the vesicle can be determined by using photon correlation spectroscopy. The morphological studies and the size distribution are characterized by laser beam spectroscopy.
MEMBRANE RIGIDITY:
Membrane rigidity can be measured by means of mobility of fluorescence probe as function of temperature.
ENTRAPMENT EFFICIENCY:
The entrapment efficiency of noisome is measured by complete vesicle disruption using 50% n-propanal and the solution is analysed by using appropriate assay method for the drug.(UV)
Entrapment efficiency = (Amount entrapped/total amount) X 100
The unentrapped drug was analysed by performing Dialysis, Gel filtration and Centrifugation.
INVITRO RELEASE STUDIES:
Invitro release study was carried out in a dialysis sac. The sac is washed and placed on distilled water. The noisome suspension was pipette into the sac and sealed. The sac was placed in 200ml of buffer solution in a 250ml beaker placed in a magnetic stirrer. On constant shaking, the samples were withdrawn at regular time intervals. The temperature maintained is 25°C to 37°C. The samples were analysed by using UV at appropriate wavelength.
STABILITY STUDIES:
The stability study was performed by storing the formulation at 3 temperature condition. The temperatures are 4°C, 25°C and 37°C in a thermostatic oven for 3 months. At regular intervals the drug content and the drug release was evaluated by studying the parameters like entrapment efficiency and *invitro* release.[12]

APPLICATIONS:
Niosomes has its applications in various fields
CANCER THERAPY:
The drugs that are mostly used in the cancer therapy through Niosomal drug delivery are Doxorubicin HCL, Methotextrate, Bleomycin, Vincristine, Daunorubicin HCL. The side effect of Doxorubicin when administered as a free drug is cardiac toxicity, whereas when administered as a niosomal formulation the cardiac toxicity was reduced. By niosomal formulation, doxorubicin has increased level in tumor cells, serum and lungs. It also reduces the proliferation rate of tumor cells and increases the life span of tumor bearing mice. Methotrexate entrapped by nisomes gives higher plasma level and also increase the half-life of drug which gives prolonged action of the drug i.e, it will have slower elimination of drug.
AS CARRIER:
Niosomes being the vesicles can easily permeate to oxygen and the hemoglobin dissociation curve is modified

similarly to non-encapsulated hemoglobin. So they are used as the carrier for hemoglobin.[13]

PER-ORAL DELIVERY:

The drugs which are degraded by the proteolytic enzymes and gastric juices cannot be administered orally. This can be modified by a niosomal formulation. Eg: Insulin is a peptide hormone which balances the glucose level in the body. It cannot be administered orally because it gets degraded by the proteolytic enzymes in the stomach. Niosomes protects the insulin from degradation by its bilayer formation.[14]

LEISHMANIASIS:

Niosomes can be used in treatment of diseases of reticulo-endothelial system. Leishmaniasis is one of the disease in which the protozoan parasites invades the liver and the spleen cells. It is treated using antimonials. These drugs as free drug cannot give increased plasma levels. Sodium stibogluconate niosomal formulation of anit-monials can permeate through the cells and target the specific cells. Thus niosomes can be used in drug targeting.[15]

OPTHALMIC DRUG DELIVERY:

The eye disorders are treated by installation of drugs through eye. It can be ophthalmic suspension, solution or an insitu-gel. Acetazolamide was prepared as niosomal preparation by using Span 60, cholesterol stearylamine (or) dicetyl phosphate. It showed better response in reduction of intraocular pressure when compared with marketed formulation (Dorzolamide). Timolol maleate (0.25%) as niosomal formulation using chitosin showed less cardiovascular side effects and effective reduction in the intra-ocular pressure.

DRUG USED IN NIOSOMAL DELIVERY WITH DIFFERENT ROUTES OF ADMINISTRARION

ROUTES OF ADMINISTRATION	EXAMPLES OF DRUG
Intravenous route	Doxorubicin, Methotrexate, Sodiumstibogluconate, Iopromide, Vincristin, Diclofenac sodium, Flurbiprofen, Centchroman, Indomethacin, Colchicine, Rifampicin, Tretinoin, Transferrin and glucose ligand, Zidovudin, Insulin, Cisplatin, Amarogentin , 5-fluorouracil, Daunorubicin, Amphotericin B, Camptothecin, Adriamycin, Cytarabine hydrochloride
Peroral route	DNA vaccines, Proteins, Peptides, Ergot alkaloid, Ciprofloxacin, Norfloxacin,Insulin
Transdermal route	Flurbiprofen, Piroxicam, Estradiol, Levonorgestrol, Nimesulide, Dithranol, Ketoconazole, Enoxacin, Ketorolac
Ocular route	Timolol maleate, Cyclopentolate
Nasal route	Sumatriptan, Influenza viral vaccine

TRANSDERMAL DRUG DELIVERY:

The delivery of drugs through skin indicates the transdermal drug delivery. The advantages of this delivery is it doesnot undergo first-pass metabolism. At the same time, the drawback of this delivery is the penetration of drugs is slow through skin. The skin acts as the barrier for the penetration of drugs this drawback can be overcome by the niosomal preparations.

MECHANISM OF NIOSOMAL SKIN DELIVERY:

The mechanism followed by the niosomes for transdermal drug delivery is:

- → Diffusion through stratum corneum layer.
- → The amount of water present in the skin is important for this mechanism.
- → The lipophilic drugs cross the stratum corneum by aggregation, fusion and adhesion.
- → The niosomes looses the cells of stratum corneum which increases the permeation of drugs.
- → The non-ionic surfactant enhances the permeation and this leads to improved drug permeation through skin.[16]

NIOSOME AS CARRIER IN DERMAL DRUG DELIVERY

Niosomes were used for the dermatological purpose in 1975 in cosmetic industry. The first niosomal cosmetic product was launched by Lancome Niosome – an anti-aging formulation.

Topical formulations of niosomes which are developed recently are mentioned below.

LOCAL ANESTHESIA:

Absence of sensation is induced by local anesthetics through topical preparation. The penetration of drug is low through skin, so niosomes acts as a carrier to improve the penetration of drug by entrapping them in vesicles which moves through the skin easily. Lidocaine hydrochloride a local anesthetic prepared by niosomes i.e, lidocane entrapped with tween20 and cholesterol showed better performance compared with liposomes.[17]

PSORIASIS:

Psoriasis is a dermal disorder, caused by a T-lympocyte-mediated autoimmune disease of dermis and epidermis. It is a chronic inflammatory condition of skin. It forms scaling erythematous plagues on skin. The patient suffers from itching, painful and disfiguring skin lesions. The drugs which are used topically for the treatment of Psoriasis are Anthralin, Methotrexate, Corticosteriods, Vit-D3, coal tar, Tacrolimus. Methotrexate is an anti-cancer drug used in the treatment of psoriasis, when administered systemically it leads to several adverse effects one which is hepatotoxicity. So, topical application can be selected as an alternate to reduce the adverse effects. The niosomal-chitosin Methotrexate gel shows 3 times reduction in lesion after 12 weeks. Thus niosomal Methotrexate gel can be used in topical treatment of psoriasis.[18]

HYPERPIGMENTATION:

Hyperpigmentation disorders can be overcome by noisomal preparation. N-acetyl glucosamine is the niosomal preparation used in treatment of hyperpigmentation as it has the potential to deliver both hydrophilic and hydrophobic drugs as topical form and also has the

property of inhibiting the thyrosine enzymes in melanocytes which treats the hyperpigmentation disorder. Gallic acid was prepared in two forms of niosomes elastic and non-elastic niosomes. The non-elastic niosme shows increased entrapment efficiency and the elastic noisome shows increased permeation through skin, which is the advantage to be used in antiaging topical application. These preparations show less toxicity and good control for availability of active ingredients at stratum corneum for moisturizing the skin.[19]

NSAIDS (Nonsteoidal Anti-inflammatory drugs)

Non-steroidal Anti-inflammatory drugs (NSAIDS) are used as analgesic and anit-inflammatory drugs. One of the NSAIDS is celecoxib, coz-2 inhibitor used in the treatment of arthritis. Arthritis is a joint disorder, inflammation found in the joints. The niosomal celecoxib gel showed 6.5 times higher drug deposition in deep skin layer and also has good permeation through skin.[20]

ACNE:

Acne is a skin disease found in 70-80% of adolescence. It can be treated by topical preparations. Niosomes can be used in topical preparations as they have efficient dermal drug delivery. Acne can be cured by both synthetic and herbal extracts. The herbal extracts have fewer side effects when compared with synthetic. Benzylperoxide a synthetic drug-macrolide antibiotic was used in the treatment of acne with other anti-acne agents. The side effects of benzyl peroxide when used as dermal delivery are itching, skin redness, irritation. Niosomal benzyl peroxide incorporated into HPMC gel was evaluated for its activity towards treatment of acne. The results showed good drug skin retention, extended release and reduced toxicity of the drug with improved drug permeation. Gallidermin- Lantibiotic has a promising dermal and cosmetic treatment for acne. It is used against the bacteria such as Propinibacterium *acnes* and Staphylococcus *aureus*. Gallidermin was prepared as anionic niosomal gallidermin composed of cholesterol/tween61/diacetylphosphate. Niosomal gallidermin gel showed more chemical stability than gallidermin aqueous gel, it showed efficient topical localization and good skin permeation without any threat to systemic circulation.[21]

CONCLUSION

Niosomal vesicular drug delivery system was concluded to be a promising dermal drug delivery system as it has good permeation of drugs through skin. Localization of drug is also found to successful which are relatively non-toxic and stable. They also present prolonged and targeted delivery of drugs as it has the potential of loading both hydrophilic and hydrophobic drugs. Niosomes were cost effective and stable in nature than liposomes. The selection of surfactant is the main parameter during formulation of niosomes, as it plays an important role in the formation of vesicles, stability and toxicity of the preparation. Other than dermal delivery it also has other types like oral, ophthalmic and parentral.

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